

would make German industries less competitive. Others, however, most remarkably including former supporters of nuclear power on the conservative side of the political spectrum, have argued that this challenge is manageable, and that the requirement to make production more energy-efficient will also give German manufacturers an advantage internationally.

A model for other countries?

Politicians and concerned citizens in other countries will observe Germany's movements closely, as it is the first example of a high technology country turning its back on nuclear energy after using it for more than half a century.

Around the world, many old and new users of nuclear reactors are sticking to their plans and policies, only adding a safety inspection here or there. At the EU level, the UK and France warned of any hasty decisions when Germany pressed for an EU-wide rethink.

China, which has 13 nuclear reactors running and 28 being built, announced it would not change its plans, but ordered safety inspections and updates to the regulations in the light of the Fukushima accident. However, as nuclear security researcher Yun Zhou wrote in a report for the Harvard Kennedy School, awareness of nuclear risks is only beginning to emerge. "More and more people are just learning of China's ambitious nuclear energy plan, which they did not pay much attention to before the Fukushima nuclear incident. Public concerns about nuclear safety could lead to questions about whether China can maintain sound nuclear safety culture and practices in light of China's poor construction safety record," Zhou concluded.

South Korea and India, each running around 20 nuclear plants and building additional ones, appear to be more worried, given their possible exposure to tsunamis. However, neither is seriously considering a change of policy. Similarly, Russia is sticking to its nuclear plants and hoping that other countries that have agreed to buy power stations from its company Rosatom will keep the faith in nuclear power as well.

Some of the new members in the nuclear club, exposed as they are

to natural and man-made disasters, would have good reasons to worry, though. An analysis carried out by *Nature* and Columbia University at New York revealed that more than 200 nuclear power plants have more people living within a 30 km radius than Fukushima-Daiichi had. In Japan, 172,000 people living less than 30 km away from the stricken reactor had to be evacuated. The record holder is a plant in Karachi, Pakistan, where 8.2 million people would have to flee in similar circumstances. Two large nuclear plants in Taiwan are less than 30 km away from the capital Taipei, which means that each has around 5 million people living within this critical radius.

So far, Switzerland is the closest to following the lead of its neighbour. The country currently produces more than half its electricity from hydroelectric generators, 40% from five nuclear plants, and small percentages from waste incineration, solar and wind power. In the wake of the Fukushima incident, the Swiss government has commissioned its environment ministry to explore a range of options, including phasing out nuclear power when the existing plants reach the end of their lifespan, and switching off nuclear plants even before their time runs out. The ministry's report is due in June and will then be subject to parliamentary debate.

As immediate measures, the Swiss government has frozen all three projects for new nuclear plants and ordered safety inspections for the existing ones.

And what about Austria? In 1978, the country held a referendum deciding not to use nuclear power. Since then, it has become Europe's leading producer of renewable energies, with 69% of its electricity produced from renewable sources, mostly hydroelectricity. If and when Germany and Switzerland switch off their reactors, Europe could end up with an enclave of German-speaking nuclear refuseniks on its map.

Maybe it's something to do with the German language. People in other countries just don't have a word for 'Energiewende'.

Michael Gross is a science writer based at Oxford. He can be contacted via his web page at www.michaelgross.co.uk

Quick guide

Lymphoid tissue inducer cells

David R. Withers

What are they? Lymphoid tissue inducer (LTi) cells are a hematopoietic cell type with critical roles in the immune system during both the embryonic and adult stages of development. Their distinguishing features are expression of ROR γ t and IL-7R α in the absence of lineage markers (e.g. CD3, CD19, B220, CD11c, Gr-1). CD4 expression is something of a red herring (despite aiding identification), since both CD4⁺ and CD4⁻ LTi cells exist in mice, whilst in humans they all appear to be CD4⁻. Constitutive expression of OX40L is another good marker for LTi cells in the adult (in mice and humans) ([Figure 1](#)).

Also known as... Although these cells were initially termed CD45⁺CD4⁺CD3⁻ cells, on the basis of the expression of these surface markers, they were named LTi cells following the recognition of their key role in the development of lymph nodes and Peyer's patches. Recently these cells have been included in the growing list of innate lymphoid cells (ILCs).

When did they first come to prominence? Although identified as one of the first cells to colonise the developing lymph node anlagen, the demonstration that these cells (and secondary lymphoid tissue) were dependent upon expression of the orphan transcription factor ROR γ t really brought LTi cells to the immunological foreground with ROR γ ^{-/-} mice providing an *in vivo* means of testing their function. The shared expression of ROR γ t by Th17 cells also sparked interest in LTi cells.

When were they in their heyday? Now! Based on the almost monthly appearances of LTi cells in papers in top journals, it appears that a good proportion of the iceberg is within sight.

Not to be confused with... A host of recent papers have identified ROR γ t-dependent cells that (to varying

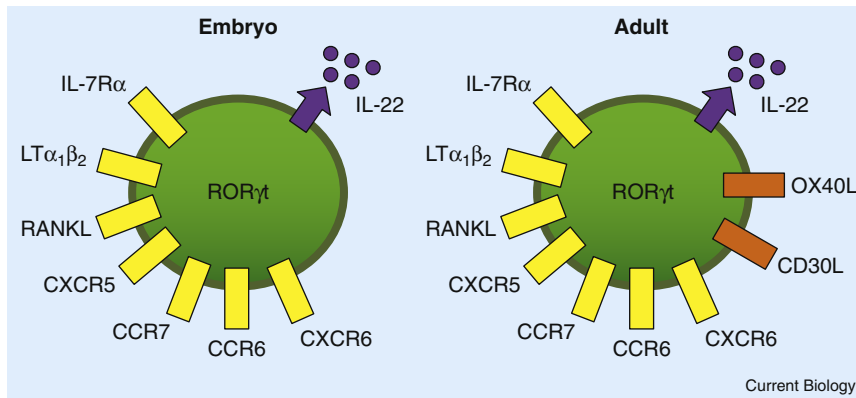


Figure 1. A selection of molecules expressed by LTi cells in the embryo and adult that appear critical for the described functions of these cells. Molecules expressed by LTi cells in both the embryo and adult are shown in yellow and those expressed only in the adult are shown in orange. Lymphotoxin $\alpha 1\beta 2$ (LT $\alpha 1\beta 2$), RANKL, OX40L and CD30L are TNF superfamily members, and CXCR5, CCR7, CCR6 and CXCR6 are chemokine receptors. IL-22, interleukin-22; IL-7R α , interleukin-7 receptor α .

degrees) are phenotypically distinct from LTi cells. These cells have only been identified within the adult, and LTi cells appear to be the only (non-T-cell) ROR γ t-expressing population in the embryo. Notably, cells with a phenotype near identical to LTi cells, but also expressing natural killer cell markers, have been reported within the small intestine. Given that these cells have not been detected in the embryo, they do not appear to be involved in secondary lymphoid tissue formation. The lineage relationships between these populations is currently being debated.

Bone of contention... Given their name, implicitly implied in their function is the ability to induce formation of secondary lymphoid tissue. Whilst LTi cells persist after birth, it is technically very difficult to demonstrate that these cells are still able to induce the formation of secondary lymphoid tissue, although it has been shown that they can induce Peyer's patch formation in neonatal mice lacking these structures. Therefore, there is some concern that the continued use of the name LTi cell, when describing these cells in the adult, may be misleading.

What was their earliest known function? LTi cells are clearly required for the formation of lymph nodes and Peyer's patches — but interestingly not for the formation of organised splenic white pulp — through the provision of the tumour necrosis factor (TNF)

superfamily ligands lymphotoxin $\alpha 1\beta 2$ and RANKL. These cells also induce the expression of the autoimmune regulator (AIRE) gene by medullary thymic epithelial cells in the developing embryonic thymus through provision of RANKL signals. Therefore, LTi cells in the embryo are the critical providers of both lymphotoxin $\alpha 1\beta 2$ and RANKL signals, before lymphocyte populations have reached the periphery.

And their newly identified functions?

Because the formation of secondary lymphoid tissue is restricted to a specific window of embryonic development, whether the LTi cells identified in the adult had acquired additional functions became of great interest. A number of studies using ROR γ t-deficient mice have implicated LTi cells in the recovery of splenic architecture after viral infection, T-cell-independent immunoglobulin A switching in the gut, and enhanced tumour rejection. Furthermore, much work has focused on the production of the interleukins IL-22 and IL-17 by LTi (and LTi-like) cells within the gut. The function of LTi cells in the embryo centres around their expression of the TNF superfamily members at a critical time and place. Interestingly, after birth LTi cells constitutively express high levels of two other TNF superfamily members — OX40L and CD30L — and become critical providers of these signals to memory CD4⁺ T cells. The formation of lymph nodes and the ability to generate memory immune responses co-evolved only within placental

mammals. Therefore, LTi cells not only orchestrate the formation of lymph nodes, but they also enable the survival of memory CD4⁺ T cells within these structures.

Most outrageous claim... A few years ago most of the current ideas about function would have been dismissed out of hand so perhaps we should wait a while longer before ruling anything out....

What are their known associates?

Stromal cells in both lymphoid tissue development and perhaps resistance to tumours. Beyond that, interactions with nearly every hematopoietic cell imaginable have been suggested.

Obvious question we still don't know the answer to...

Given the similarities between the development of secondary lymphoid tissue and the formation of organised lymphoid aggregates during chronic inflammations, a role for LTi cells in the establishment of tertiary lymphoid tissue is suspected but as yet unproven.

Any therapeutic potential? The role of LTi cells (and OX40L/CD30L) in the survival of memory CD4⁺ T cells has significant implications for improving desired memory responses after vaccination as well as in the potential elimination of autoreactive cells.

Where can I find out more?

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MRC Centre for Immune Regulation, School of Medical and Dental Sciences, University of Birmingham, Birmingham B15 2TT, UK.
E-mail: d.withers@bham.ac.uk